BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

ZEPBOUND® (tirzepatide) subcutaneous injection for obstructive sleep apnea (OSA) Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and/or Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Medical Necessity Requirements for ZEPBOUND (tirzepatide)

Purpose: This coverage guideline is used to review Zepbound use in established obstructive sleep apnea (OSA). For use in weight loss, please refer to the member's benefit plan book.

Criteria for Initial Therapy:

Note: Check benefit book to make sure there are no benefit or contract exclusions that apply.

Prescriber Qualifications
- Prescribed by a Pulmonologist or Sleep Medicine Physician, or in consultation with one

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Indication
- Moderate to severe obstructive sleep apnea in an individual with obesity

Age Requirement
- 18 years or older

Baseline Clinical Evaluation
- Apnea Hypopnea Index greater than 15 events/hour on polysomnogram
- Body mass index of 95th percentile or greater, or body mass index 30 kg/m² or greater

Alternative Therapies
- Paid claims or submission of medical records (e.g., chart notes) confirming failure (trial for at least three months duration), contraindication, or intolerance to **ONE** of the following non glucagon like peptide 1 receptor agonist weight loss medication:
  - Contrave (bupropion / naltrexone)
  - Orlistat (Alli, Xenical)
  - Phentermine
  - Qsymia (phentermine / topiramate extended release)

Brand Specific Criteria
- Have failure, contraindication, or intolerance with **THREE** generic equivalents (if available) for at least three months each. **Note**: Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

Safety
- No concomitant use with glucagon like peptide 1 agonists (e.g., Ozempic, Rybelsus, Trulicity, Mounjaro)
- No FDA labeled contraindications such as:
  - Personal or family history of medullary thyroid carcinoma
  - Multiple Endocrine Neoplasia syndrome type 2
  - Prior serious hypersensitivity reaction (e.g., anaphylaxis, angioedema) to GLP 1 receptor agonists (e.g., Ozempic, Rybelsus, Trulicity, Mounjaro)
- Does not have **ANY** of the following:
  - Severe gastrointestinal disease including severe gastroparesis
  - Suicidal behavior or ideation
  - Signs and symptoms of pancreatitis
  - Gallbladder disease (e.g., cholelithiasis, cholecystitis)
  - Pregnancy

Additional Requirements
- Is participating in a program that supports a reduced calorie diet, at least 500 kcal/day reduction in intake, and physical activity of at least 150 minutes per week
- Does not have diagnosis of diabetes mellitus type 1 or type 2, history of ketoacidosis, hyperosmolar state/coma, or Hemoglobin A1c greater than 6.5 percent
- Not solely used for weight loss; must also be on appropriate therapy for obstructive sleep apnea
- Using Positive Airway Pressure (PAP) therapy unless medically contraindicated due to:
  - Skin reactions or irritation
  - Nasal polyposis, congestion, or dryness unresponsive to nasal therapies

- Eye irritation from pressurized air
- Aerophagia
- Air leakage around device
- Psychosocial issues (e.g., claustrophobia, psychiatric disorders)
- Other physical limitations (e.g., arthritis, muscle weakness)

Documentation Requirements

- A completed request form must be submitted including:
  - Chart notes
  - Lab results (Apnea Hypopnea Index values)
  - Supporting clinical documentation

Initial Therapy Criteria Approval Duration

- 6 months OR end of plan year

Criteria for Continuation of Therapy (renewal therapy):

Note: Manufacturer assistance (e.g., coupons, samples, etc.) are not considered for continuation of therapy.

Prescriber Qualifications

- Continues to be seen by a Pulmonologist or Sleep Medicine Physician, or in consultation with one

Clinical Response

- **BOTH** of the following:
  - Improvement in Apnea Hypopnea Index over baseline
  - Reduction of 5 percent or more in body weight from baseline

Adherence

- Adherence to the prescribed therapy regimen has been documented
- Continues reduced calorie diet (at least 500 kcal/day reduction) and physical activity (at least 150 minutes/week)

Brand Specific Criteria

- Have failure, contraindication, or intolerance with **THREE** generic equivalents (if available) for at least three months each. **Note**: Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

Safety

- No concomitant use with glucagon like peptide 1 agonists (e.g., Ozempic, Rybelsus, Trulicity, Mounjaro)
- No new contraindications or significant adverse drug effects such as:
  - Pancreatitis
  - Severe hypersensitivity reaction
  - Acute kidney injury
  - Severe gastrointestinal disease
  - Drug induced immune mediated thrombocytopenia
  - Acute gallbladder disease
- Does not have **ANY** of the following:

  - Severe gastrointestinal disease including severe gastroparesis
  - Suicidal behavior or ideation
  - Signs and symptoms of pancreatitis
  - Gallbladder disease
  - Pregnancy
- Not currently taking any other drugs causing severe adverse reactions requiring discontinuation

Additional Requirements

- No diagnosis of diabetes mellitus type 1 or type 2, history of ketoacidosis, hyperosmolar state/coma, or Hemoglobin A1c less than 6.5 percent
- Not solely used for weight loss; must also be on appropriate therapy for obstructive sleep apnea
- Using Positive Airway Pressure (PAP) therapy unless medically contraindicated

Documentation Requirements

- Chart notes
- Supporting clinical documentation with evidence of improvement in obstructive sleep apnea
- Lab values confirming safe use

Continuation Therapy Criteria Approval Duration

- 12 months OR end of plan year

Criteria for Off-Label Use Requests:

Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. Off-Label Use of Non-Cancer Medications

2. Off-Label Use of Cancer Medications

Description:

Zepbound (tirzepatide) is a glucose-dependent insulinotropic polypeptide (GIP) receptor and glucagon-like peptide-1 (GLP-1) receptor agonist indicated in combination with a reduced-calorie diet and increased physical activity to treat moderate to severe obstructive sleep apnea (OSA) in adults with obesity.

OSA is the most common type of sleep apnea and is characterized by repeated episodes of complete or partial obstructions of the upper airway during sleep despite the effort to breathe, and is usually associated with a reduction in blood oxygen saturation. In OSA, the episodes of decreased breathing are called “hypopnea” (defined as a ≥ 30% drop in flow for 10 seconds or longer, associated with ≥ 3% oxygen desaturation). The episodes of breathing cessations are called “apneas” (literally, “without breath”) and are defined, as a ≥ 90% drop in flow for 10 seconds or longer and associated with ≥3 % oxygen desaturation, or an arousal. The number of events per hour are measured and reported as an apnea hypopnea index (AHI).

Moderate to severe OSA, can also be defined as a respiratory disturbance index [RDI] greater than 15 events per hour. Like the AHI, RDI reports on respiratory events during sleep, but unlike AHI, it also includes respiratory-effort related arousals (RERAs). RERAs are arousals from sleep that do not technically meet the definitions of apneas or hypopneas, but do disrupt sleep. They are abrupt transitions from a deeper stage of sleep to a shallower stage. RERA is characterized by increasing respiratory effort (and thus decreasing esophageal pressures) for 10 seconds or more leading to an arousal from sleep, but one that does not fulfill the criteria for a hypopnea or apnea.

Positive airway pressure (PAP) is the treatment of choice for an individual with OSA. A maximal effort to treat OSA with PAP for an adequate period of time should be made prior to initiating pharmacologic therapy.

Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

Apnea Hypopnea Index (AHI):

- The AHI is the number of apneas or hypopneas events per hour of sleep (i.e., apneas + hypopneas/total sleep time in hours)
- It is a measure sleep apnea severity; the apnea must last for at least 10 seconds and be associated with a decrease in blood oxygenation
- Based on the AHI, the severity of OSA is classified as follows:
  - None/Minimal: AHI < 5 per hour
  - Mild: AHI ≥ 5, but < 15 per hour
  - Moderate: AHI ≥ 15, but < 30 per hour
  - Severe: AHI ≥ 30 per hour

Respiratory Disturbance (or distress) Index (RDI):

- Like AHI, it reports on respiratory events during sleep, but unlike AHI, it also includes respiratory-effort related arousals (RERAs) (i.e., (apneas + hypopneas + RERAs/total sleep time in hours)
- RERAs are arousals from sleep that do not technically meet the definitions of apneas or hypopneas but do disrupt sleep. They are abrupt transitions from a deeper stage of sleep to a shallower stage
  - A RERA is characterized by increasing respiratory effort (and thus decreasing esophageal pressures) for 10 seconds or more leading to an arousal from sleep, but one that does not fulfill the criteria for a hypopnea or apnea
- Respiratory Event Index (REI) = apneas + hypopneas/total recording time

Diagnosis obstructive sleep apnea		
Sleep testing device	Index	Diagnostic criteria for OSA
Polysomnography*	Apnea Hypopnia Index (AHI)	AHI 5-14/hour sleep **PLUS** one or more sleep-associated conditions¶ **or** AHI ≥15/hour sleep

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	Respiratory Disturbance Index (RDI)	RDI 5-14/hour sleep **PLUS** one or more sleep associated conditions¶ **or** RDI ≥15/hour sleep
Home sleep apnea device	Respiratory Event Index (REI)	REI ≥15/hour total recording time

* Most polysomnography studies will report AHI, RDI, or both values
¶ Sleep-associated conditions include the following:

- Sleepiness, nonrestorative sleep, fatigue, or insomnia symptoms
- Waking up with breath holding, gasping, or choking
- Habitual snoring, breathing interruptions, or both noted by a bed partner or other observer
- Hypertension, mood disorder, cognitive dysfunction, CAD, stroke, CHF, atrial fibrillation, or type 2 DM

Resources:

Zepbound (tirzepatide) subcutaneous injection product information, revised by Eli Lilly and Company. 04-2025. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed November 07, 2025.

Kline LR. Clinical presentation and diagnosis of obstructive sleep apnea in adults. In: UpToDate, Collop N, Finlay G (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through November 2025. Topic last updated November 25, 2025. Accessed December 11, 2025.

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Pepin JL. Evaluations and management of residual excessive sleepiness in adults with obstructive sleep apnea. In: UpToDate, Collop N, Scammell TE, Finlay G (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through November 2025. Topic last updated September 15, 2025. Accessed December 11, 2025.

Malhotra A, Grunstein RR, Fietze I, et al.: Tirzepatide for the treatment of obstructive sleep apnea and obesity. NEJM 2024 Oct 3;391(13):1193-1205. Accessed February 07, 2025.